

REMARKS/ARGUMENTS

The Office Action rejected claims 39-58 under 35 U.S.C. §101 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-15, and 18-24 of U.S. Patent No. 6,361,947 B1. Claims 39, 44, 45 and 45-48 were rejected under 35 U.S.C. §102 over McCaskey Feazel et al. U.S. Patent No. 6,100,030 and claims 40-43, 46, 47 and 56 were rejected under 35 U.S.C. §103 using McCaskey Feazel in view of DeRisi et al. (*Science*, 278:680-686).

Applicants note that the Examiner has indicated that claims 57 and 58 are free of prior art. Claim 57 has been amended so that it is independent form.

Rejection under 35 USC §101

Claims 39-58 have been rejected under obviousness-type double patenting over claims 1-8, 11-15 and 18-24 of U.S. Patent No. 6,361,947. Applicants have filed a terminal disclaimer herewith. Therefore Applicants believe that this rejection should be removed.

Rejection under 35 USC §102

Claims 39, 44, 45, and 48-55 have been rejected over McCasky Feazel et al. U.S. Patent No. 6,100,030. Claims 54 and 55 have been canceled. Claim 39 as amended is drawn to a method of analyzing a first nucleic acid sample by fragmenting the sample, ligating adaptors to the fragments and amplifying the fragments so that a subset of the fragments is enriched in the resulting second nucleic acid sample. A computer is used to predict the fragments that will be enriched in the subset given the method of fragmenting and amplifying that are used. The fragments are hybridized to an array of probes that are complementary to fragments that are predicted to be enriched in the subset. Support for these amendments may be found in claims 54-56 as filed.

Amended claim 39 combines a method of generating an amplified nucleic acid sample with a method to design an array that uses a computer system. Different methods of fragmentation and amplification may be selected, the computer system is used to predict the fragments that will be amplified and the array is designed to detect at least

some of those fragments. The array ideally will have probes to only a subset of the entire genome of the organism—that subset that the computer predicts will be amplified when the selected fragmentation and amplification methods are used. The fragmentation and amplification method chosen dictates the probes of the array.

A computer system is used to predict the size and sequence of fragments resulting from a fragmentation method and then to predict which of those fragments will be amplified by the selected amplification method. Probes that are complementary to those fragments are then synthesized on the array.

On page 6 of the office action the Examiner recognizes that McCasky Feazel et al. do not teach a method of determining the sequence of the probes by a computer system. Applicants would like to clarify that not only is a computer system used to determine the probes of the array, but a computer system is also used to predict the fragments that will be present in the second nucleic acid sample. The method of claim 39 uses a computer to predict the fragments that will be amplified under selected fragmentation and amplification methods, thus predicting the fragments that will be in the second nucleic acid sample and not simply to determine probe sequences for the array. A researcher selects the fragmentation method, for example, a specific restriction enzyme, and uses the computer to model fragmentation of the genome by the enzyme, thus predicting the size and sequence of all fragments. The researcher then determines the size of the fragments that will be efficiently amplified using a selected amplification method, for example, PCR. This identifies a subset of fragments that will be enriched in the amplified product. The researcher may then identify sequences of interest, for example, SNPs on fragments that are predicted to be in the subset of fragments that is enriched. The computer may be used to identify those fragments in the subset that contain a sequence of interest, for example, a SNP. The array may be designed, for example, to genotype SNPs on fragments that are predicted to be in the amplified product. McCasky Feazel does not teach this method and it is not an obvious modification of the method of McCasky Feazel et al. In fact, McCasky Feazel et al. teaches an empirical method of identifying target sequences using amplified fragment length polymorphisms, see column 8, lines 9-16 and lines 57-63.

For the above reasons, Applicants believe these rejections should be removed. Applicants have also amended claims 40-43 to clarify that the percentage refers to amplification of complete fragments, but of only a subset of the total number of fragments.

Rejection under 35 USC §103

Claims 40-43, 46, 47 and 56 have been rejected over McCasky Feazel et al. in view of DeRisi et al. Claim 56 has been canceled making this rejection moot. Claims 40-43, 46 and 47 are dependent on amended claim 39. For the reasons discussed above McCasky Feazel et al. fails to teach a method of using a computer to predict the fragments that will be amplified when a selected fragmentation and amplification method are used and designing an array to detect at least some of the predicted fragments. DeRisi et al. also fails to disclose methods of using a computer to predict the fragments in a second amplified nucleic acid sample and the design of an array to detect those predicted fragments. Therefore, Applicants believe these rejections should be removed.

CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. Applicants believe that no extension of time is required for submission of this paper. However, if an extension is required, Applicants petition for any necessary extension of time and authorize the Commissioner to deduct any required fees from the undersigned's Deposit Account No. 01-0431. Please deduct any additional fees from, or credit any overpayment to the above-noted Deposit Account. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5768.

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Respectfully submitted,



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